



Applicants : Carolyn E. Mountford et al.
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Filed : October 18, 2000 Examiner: Arlen Soderquist
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This listing of claims will replace all prior versions, and listings, of claims in this application:

Listing of Claims

1. (Currently Amended) A method for obtaining a statistical classifier for classifying spectral data from a biopsy of breast tissue to determine the classification of a characteristic of the breast tissue, comprising:
 - (a) locating a plurality of maximally discriminatory subregions in magnetic resonance spectra of biopsies of breast tissue having known classifiers of a characteristic,
 - (b) cross-validating the spectra by selecting a first portion of the spectra comprising about one-half of the spectra leaving the other one-half of the spectra in the remainder of the spectra, developing linear discriminant analysis classifiers from said first portion of spectra, and validating the remainder of the spectra using the classifiers from the first portion of the spectra, to obtain optimized linear discriminant analysis coefficients,
 - (c) repeating step (b) a plurality of times, each time selecting a different portion of the spectra, to

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obtain a different set of optimized linear discriminant analysis coefficients for each of said plurality of times; and

(d) obtaining a weighted average of the linear discriminant analysis coefficients to obtain final classifier spectra indicating the classification of the characteristic based on the spectra; [and (e) comparing] wherein spectra from a biopsy of breast tissue of unknown classification of a characteristic may be compared to the final classifier spectra to determine the classification of the characteristic of the breast tissue.

2. (Original) The method of claim 1 wherein the step of cross-validating the spectra comprises cross-validating the spectra by randomly selecting about half of the spectra.

3. (Original) The method of claim 1, further including the step of obtaining a biopsy of breast tissue by a fine needle aspiration biopsy.

4. (Original) The method of claim 1, wherein the step of repeating step (b) a plurality of times comprises repeating

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step (b) about 500-1000 times.

5. (Original) The method of claim 1, further including the steps of obtaining a plurality of final classifier spectra independently, and aggregating the results of the independent classifiers to obtain a consensus diagnosis.
6. (Original) The method according to claim 1, wherein the characteristic is pathology of the breast tissue and the classification indicates whether the pathology is malignant, benign or normal.
7. (Original) The method according to claim 1, wherein the characteristic is tumor vascularization, and the classification indicates the extent of tumor vascularization.
8. (Original) The method according to claim 1, wherein the characteristic is tumor nodal involvement and the classification indicates the extent of tumor nodal involvement.
9. (Currently amended) An apparatus for obtaining a statistical classifier for classifying spectral data from a

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biopsy of breast tissue to determine the classification of a characteristic of the breast tissue, comprising:

- (a) a locator for locating a plurality of maximally discriminatory subregions in magnetic resonance spectra of biopsies of breast tissue having known classifiers of a characteristic of breast tissue,
- (b) a cross-validator for selecting a first portion of the spectra comprising about one-half of the spectra leaving the other one-half of the spectra in the remainder of the spectra, developing linear discriminant analysis classifiers from said first portion of spectra, and validating the remainder of the spectra using the classifiers from the first portion of the spectra, to obtain optimized linear discriminant analysis coefficients, said cross-validator selecting, developing and validating a plurality of times, each time selecting a different portion of the spectra, to obtain a different set of optimized linear discriminant analysis coefficients for each of said plurality of times, and
- (c) an averager for obtaining a weighted average of the linear discriminant analysis coefficients to obtain

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final classifier spectra indicating the classification of the characteristic based on the spectra, whereby spectra from a biopsy of breast tissue of unknown classification of a characteristic may be compared to the final classifier spectra to determine the classification of the characteristic of the breast tissue.

10. (Original) The apparatus of claim 9 wherein the cross-validator randomly selects about half of the spectra.
11. (Original) The apparatus of claim 9, wherein the cross-validator repeats step (b) about 500-1000 times.
12. (Original) The apparatus of claim 9, wherein the characteristic is pathology of the breast tissue and the classification indicates whether the pathology is malignant, benign or normal.
13. (Original) The apparatus of claim 9, wherein the characteristic is tumor vascularization, and the classification indicates the extent of tumor vascularization.
14. (Original) The apparatus of claim 9, wherein the

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characteristic is tumor nodal involvement and the classification indicates the extent of tumor nodal involvement.

15. (Currently Amended) A. method for determining the classification of a characteristic of breast tissue, comprising:

obtaining magnetic resonance spectra of a biopsy of breast tissue having unknown classification of a characteristic and comparing the spectra with a classifier, said classifier having been obtained by:

- (a) locating a plurality of maximally discriminatory subregions in the magnetic resonance spectra of biopsies of breast tissue having known classifications of a characteristic of the breast tissue,
- (b) cross-validating the spectra of (a) by selecting a first portion of spectra comprising about one-half of the spectra leaving the other one-half of the spectra in the remainder of the spectra, developing linear discriminant analysis classifier from said first portion of spectra, and validating the remainder of the spectra using the classifications from the first portion of the spectra, to obtain optimized linear

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discriminant analysis coefficients,

- (c) repeating step (b) a plurality of times, each time selecting a different portion of the spectra, to obtain a different set of optimized linear discriminant analysis coefficients for each of said plurality of times, and
- (d) obtaining a weighted average of the linear discriminant analysis coefficients to obtain final classifier spectra indicating the classification of the characteristic based on the spectra, and comparing the spectra from the biopsy of breast tissue having unknown classification to the final classifier spectra to determine the classification of the characteristic of the breast tissue.

16. (Original) The method of claim 15, wherein the characteristic is pathology of the breast tissue and the classification indicates whether the pathology is malignant, benign or normal.

17. (Original) The method of claim 15, wherein the characteristic is tumor vascularization, and the classification indicates the extent of tumor

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vascularization.

18. (Original) The method of claim 15, wherein the characteristic is tumor nodal involvement and the classification indicates the extent of tumor nodal involvement.

19. (Currently Amended) An apparatus for determining the classification of a characteristic of breast tissue, comprising:

a spectrometer for obtaining magnetic resonance spectra of a biopsy of breast tissue having unknown classification of a characteristic;

a classifier for statistically classifying the spectra by comparing the spectra with a reference classifications, said classifier having been obtained by:

(a) locating a plurality of maximally discriminatory subregions in the magnetic resonance spectra of biopsies of breast tissue having known classifications of a characteristic of the breast tissue,

(b) cross-validating the spectra of (a) by selecting a first portion of spectra comprising about one-half of the spectra leaving the other one-half of the spectra

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in the remainder of the spectra, developing linear discriminant analysis classifier from said first portion of spectra, and validating the remainder of the spectra using the classifiers from the first portion of the spectra, to obtain optimized linear discriminant analysis coefficients,

- (c) repeating step (b) a plurality of times, each time selecting a different portion of the spectra, to obtain a different set of optimized linear discriminant analysis coefficients for each of said plurality of times, and
- (d) obtaining a weighted average of the linear discriminant analysis coefficients to obtain final classifier spectra indicating the classification of the characteristic based on the spectra, and wherein said classifier compares the spectra from the biopsy of breast tissue having unknown classification to the final classifier spectra to determine the classification of the characteristic of the breast tissue.

20. (Original) The apparatus according to claim 19, wherein the characteristic is pathology of the breast tissue and the classification indicates whether the pathology is

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malignant, benign or normal.

21. (Original) The apparatus according to claim 19, wherein the characteristic is tumor vascularization, and the classification indicates the extent of tumor vascularization.
22. (Original) The apparatus according to claim 19, wherein the characteristic is tumor nodal involvement and the classification indicates the extent of tumor nodal involvement.
23. (Currently amended) A method for obtaining a statistical classifier for classifying spectral data from a biopsy of tissue to determine the classification of a characteristic of the tissue, comprising:
 - (a) locating a plurality of discriminatory subregions in magnetic resonance spectra of biopsies of tissue having known classifiers of a characteristic,
 - (b) cross-validating the spectra by selecting a first portion of the spectra comprising about one-half of the spectra leaving the other one-half of the spectra in the remaining portion of the spectra, developing

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linear discriminant analysis classifiers from said first portion of spectra, and validating the remainder of the spectra using the classifiers from the first portion of the spectra, to obtain optimized linear discriminant analysis coefficients,

(c) repeating step (b) a plurality of times, each time selecting a different portion of the spectra, to obtain a different set of optimized linear discriminant analysis coefficients for each of said plurality of times; and

(d) obtaining a weighted average of the linear discriminant analysis coefficients to obtain final classifier spectra indicating the classification of the characteristic based on the spectra, wherein spectra from a biopsy of tissue of unknown classification of a characteristic may be compared to the final classifier spectra to determine the classification of the characteristic of the tissue.

24. (Currently amended) An apparatus for obtaining a statistical classifier for classifying spectral data from a biopsy of tissue to determine the classification of a characteristic of the tissue, comprising:

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- (a) a locator for locating a plurality of discriminatory subregions in magnetic resonance spectra of biopsies of tissue having known classifiers of a characteristic of tissue,
- (b) a cross-validator for selecting a first portion of the spectra comprising about one-half of the spectra leaving the other one-half of the spectra in the remaining portion of the spectra, developing linear discriminant analysis classifiers from said first portion of spectra, and validating the remainder of the spectra using the classifiers from the first portion of the spectra, to obtain optimized linear discriminant analysis coefficients, said cross-validator selecting, developing and validating a plurality of times, each time selecting a different portion of the spectra, to obtain a different set of optimized linear discriminant analysis coefficients for each of said plurality of times, and
- (c) an averager for obtaining a weighted average of the linear discriminant analysis coefficients to obtain final classifier spectra indicating the classification of the characteristic based on the spectra,

whereby spectra from a biopsy of tissue of unknown classification of a characteristic may be compared to the

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final classifier spectra to determine the classification of the characteristic of the tissue.

25. (Currently amended) A method for determining the classification of a characteristic of tissue, comprising: obtaining magnetic resonance spectra of a biopsy of tissue having unknown classification of a characteristic and comparing the spectra with a classifier, said classifier having been obtained by:

- (a) locating a plurality of discriminatory subregions in the magnetic resonance spectra of biopsies of tissue having known classifications of a characteristic of the tissue,
- (b) cross-validating the spectra of (a) by selecting a first portion of spectra comprising about one-half of the spectra leaving the other one-half of the spectra in the remainder of the spectra, developing linear discriminant analysis classifier from said first portion of spectra, and validating the remainder of the spectra using the classifications from the first portion of the spectra, to obtain optimized linear discriminant analysis coefficients,
- (c) repeating step (b) a plurality of times, each time selecting a different portion of the spectra, to

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obtain a different set of optimized linear discriminant analysis coefficients for each of said plurality of times, and

(d) obtaining a weighted average of the linear discriminant analysis coefficients to obtain final classifier spectra indicating the classification of the characteristic based on the spectra, wherein the spectra from the biopsy of tissue having unknown classification may be compared to the final classifier spectra to determine the classification of the characteristic of the tissue.

26. (Currently amended) An apparatus for determining the classification of a characteristic of tissue, comprising: a spectrometer for obtaining magnetic resonance spectra of a biopsy of tissue having unknown classification of a characteristic;

a classifier for statistically classifying the spectra by comparing the spectra with a reference classifications, said classifier having been obtained by:

(a) locating a plurality of maximally discriminatory subregions in the magnetic resonance spectra of biopsies of tissue having known classifications of a

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characteristic of the tissue,

- (b) cross-validating the spectra of (a) by selecting a first portion of spectra comprising about one-half of the spectra leaving the other one-half of the spectra in the remainder of the spectra, developing linear discriminant analysis classifier from said first portion of spectra, and validating the remainder of the spectra using the classifiers from the first portion of the spectra, to obtain optimized linear discriminant analysis coefficients,
- (c) repeating step (b) a plurality of times, each time selecting a different portion of the spectra, to obtain a different set of optimized linear discriminant analysis coefficients for each of said plurality of times, and
- (d) obtaining a weighted average of the linear discriminant analysis coefficients to obtain final classifier spectra indicating the classification of the characteristic based on the spectra, and wherein said classifier compares the spectra from the biopsy of tissue having unknown classification to the final classifier spectra to determine the classification of the characteristic of the tissue.